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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/756,978	01/09/2001	Eugene Roussel	210582.0001/1US	6809

570 7590 12/10/2001

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EXAMINER
DAVIS, NATALIE A

ART UNIT	PAPER NUMBER
1642	8

DATE MAILED: 12/10/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/756,978	Applicant(s) ROUSSEL, EUGENE	
	Examiner Natalie A. Davis	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-67 and 73* is/are pending in the application.

4a) Of the above claim(s) *67 and 73* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's cancellation of claims 68-72 and 74-80 and election without traverse of Group I, claims 1-66 in Paper No. 7 is acknowledged.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-66 are being examined as belonging to the elected Group I, while claims 67 and 73 are withdrawn from examination as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-66 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

3. The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir., 1988). They include: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are drawn to a method of alleviating a tumor comprising administering to the tumor an antigen-releasing agent, leukocyte attractants, inflammatory response promoting agents, memory cell-inducing agents, and nutrients.

The specification discloses an antigen-releasing agent as: a proteolytic enzyme, an apoptosis inducing agent, electrical current, a strong acid, and a strong base (p. 4). A leukocyte attractant is defined as: RANTES, IP-10, and Mig, a memory cell-inducing agent as: IL-15 or interferon-alpha, and a nutrient as: vitamins A, B, C, D, and D and minerals selenium, zinc, calcium, magnesium, iron and copper (p. 5). The disclosure defines inflammatory response promoting agents as interferon-gamma, IL-2, and tumor necrosis factor-beta (p. 10). The specification gives examples of how the invention may be practiced as a result of the teaching provided within (p. 24-26).

The instant disclosure fails to meet the enablement requirement for the following reasons:

The nature of the invention is a method of alleviating a tumor. Mori, et al. (1993), Zeisig, et al., (1994), Wuyts, et al. (1994), Akatov, et al. (2000), and Schrauzer, et al. (2000) are cited in order to establish the general state of the art and level of predictability of alleviating a tumor in a human patient as claimed. Mori, et al. disclose the antiproliferative effects of interferon gamma, an inflammatory response agent, on human endometrial carcinoma cell lines, Zeisig, et al. disclose the cytotoxic effects of alklphosphocholines, an antigen-releasing agent, on tumors, Wuyts, et al. disclose the immunological importance of leukocyte attractants MCP-1-3 in cancer, Akatov, et al. disclose that vitamins B12b and C can cause death of tumor cells, and Schrauzer, et al. discloses that selenium exerts anticarcinogenic effects. However, the prior art does not disclose tumor alleviation in a human by administration of an antigen-releasing agent, leukocyte attractants, inflammatory response promoting agents, memory cell-inducing agents, and nutrients, or any combination thereof. The specification gives examples of two variations of how the invention may be practiced, but does not exemplify tumor alleviation using the method as claimed. The disclosure does not give any definitive evidence that administering the claimed agents alleviates tumors in humans. Furthermore, the predictability of alleviating a tumor in a human is uncertain because the prior art indicates that the agents may kill tumor cells *in vitro* and not tumors in human patients.

An article by *Dermer (BIO/TECHNOLOGY, Vol 12, page 320, 03/1994*) is cited in order to establish the general state of the art and the level of predictability of *in vivo* therapy. Dermer teaches that "What is significant in culture, for example immunotherapy's killing power or the transformation of 3T3 cells by a mutated proto-oncogene, simply does not have the same

significance for cells in vivo." Those of skill in the art recognize that, although *in vitro* assays are generally useful to screen the effects of agents on target cells, clinical correlation with treatment of a disease *in vivo* does not necessarily follow. The greatly increased complexity of *in vivo* therapy compared to the narrowly defined and controlled conditions of an *in vitro* assay does not permit a direct extrapolation of *in vitro* assay results to mammal or human therapy with any degree of predictibility. *In vitro* assays cannot adequately assess cell to cell interactions which may be important in a particular pathological state. Furthermore, a therapeutic agent must accomplish several tasks to be effective; it must be delivered into circulation, it must interact at the proper site at a therapeutic concentration, and it must remain effective for a sufficient period of time. *In vitro* assays cannot duplicate the complex conditions of *in vivo* therapy. In an *in vitro* assay, the agent is in direct contact with target cells during the entire exposure period, whereas in *in vivo* therapy, exposure at the target site may be delayed and/or reduced. The composition may be inactivated *in vivo*, such as by proteolytic degradation or immunological inactivation, before producing the desired effect. See Jain et al., Cancer and Metatasis Review, vol. 9, pp. 253-266, for a discussion of the differences between *in vitro* assay and *in vivo* therapy and the numberous pitfalls associated with *in vivo* cancer therapy. Accordingly, it would be unpredictable to practice the invention as claimed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Natalie A. Davis whose telephone number is 703-308-6410. The examiner can normally be reached on M-F 8-5:30 (every other Friday off).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4315 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Natalie A. Davis, Ph.D.
November 28, 2001